Rapid HIV Testing: 2004 Update

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MMWR

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Advancing HIV Prevention: New Strategies for a Changing Epidemic — United States, 2003

In several U.S. cities, recent outbreaks of primary and secondary syphilis among men who have sex with men (MSM) (*1*) and increases in newly diagnosed human immunodeficiency virus (HIV) infections among MSM and among heterosexuals have created concern that HIV incidence might be increased rapidly during the 1980s. During 1981–2001, an estimated 1.3–1.4 million persons in the United States were infected with HIV (*3*), and 816,149 cases of AIDS and 467,910 deaths were reported to CDC (*4*). During the late 1990s, after the introduction of combination antiretroviral

Why a New Initiative

- Stable morbidity and mortality
- Concerns about possible increases in HIV incidence
- Lack of knowledge of serostatus
- Effect of knowledge of serostatus on behavior
- Availability of a simple, rapid HIV test

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Estimated Awareness of Serostatus among Persons with HIV, United States

Number HIV infected	850,000 - 950,000
Number unaware of their HIV infection	180,000 - 280,000

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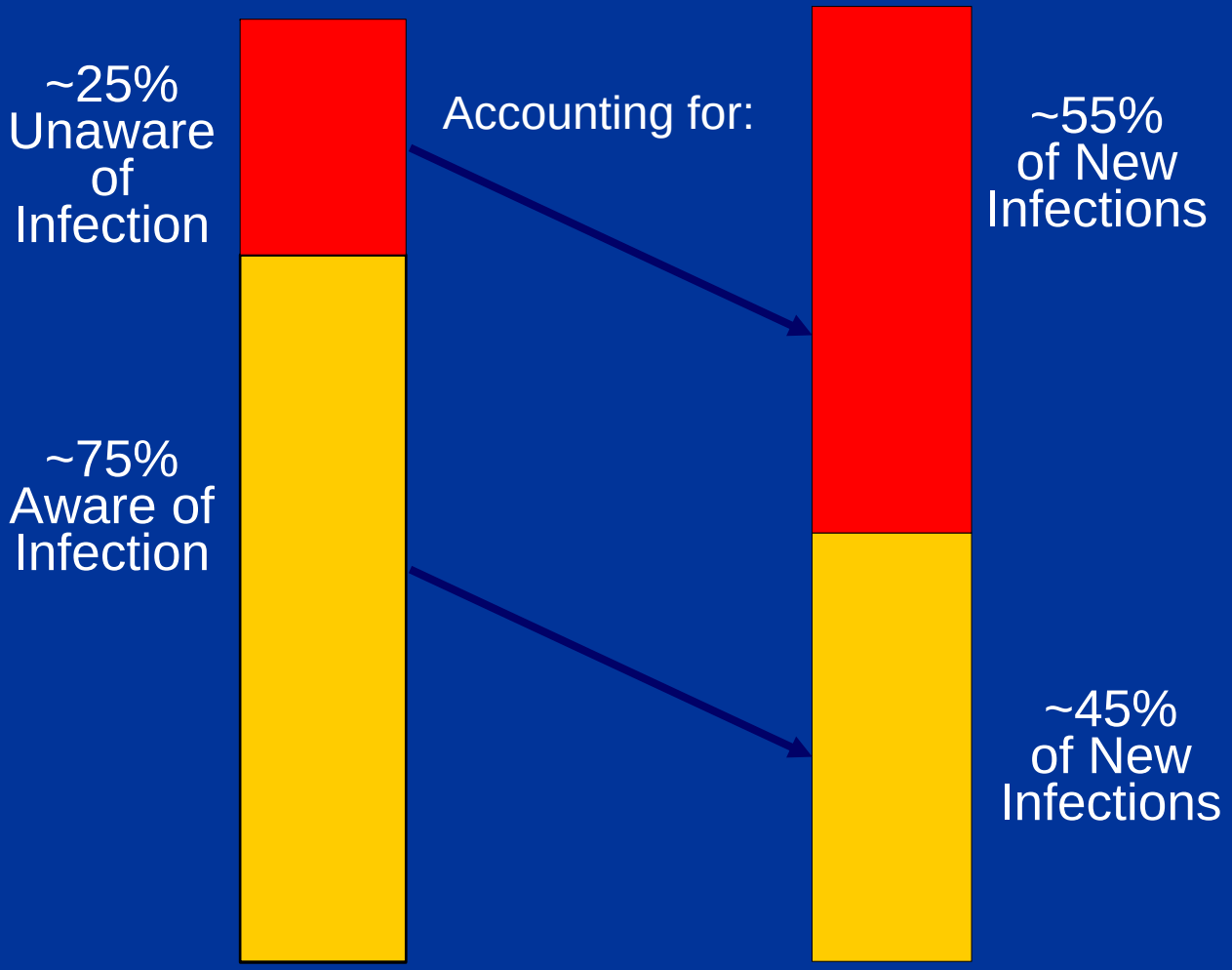
Awareness of Serostatus Among People with HIV and Estimates of Transmission



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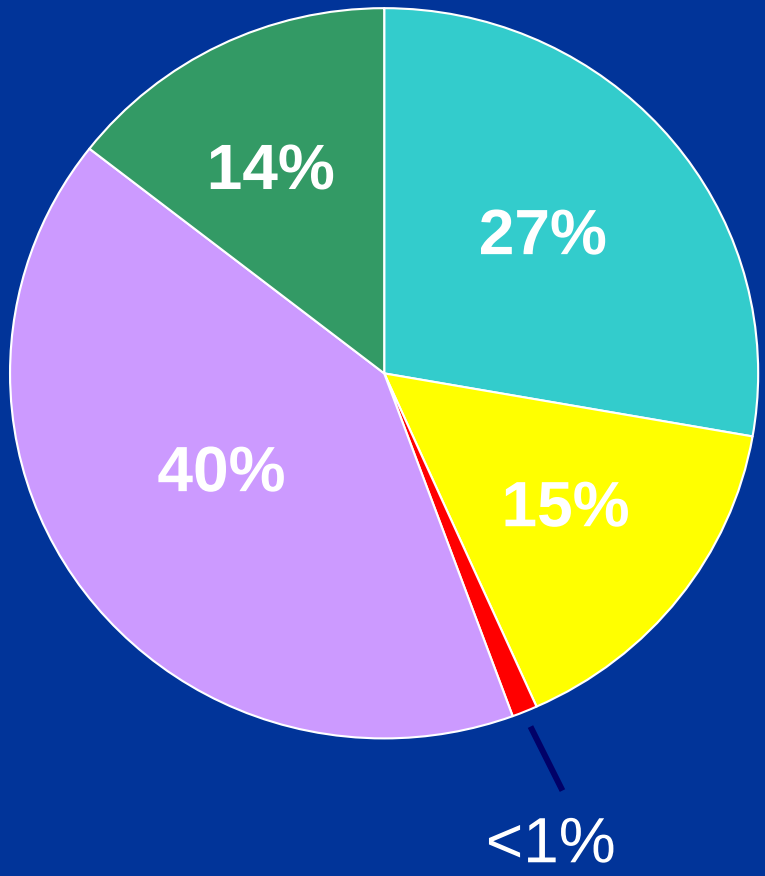
Sexual Behaviors of 1,606 HIV-Infected Persons* Interviewed in SHAS, 2002



- Abstinent
- Sex with single HIV-positive partner only
- Sexually active, no vaginal or anal intercourse at last encounter
- Only protected vaginal or anal intercourse at last encounter
- Any unprotected vaginal or anal intercourse at last encounter

* Sexual behavior in the last 12 months among persons who knew their serostatus for 12 months or more.

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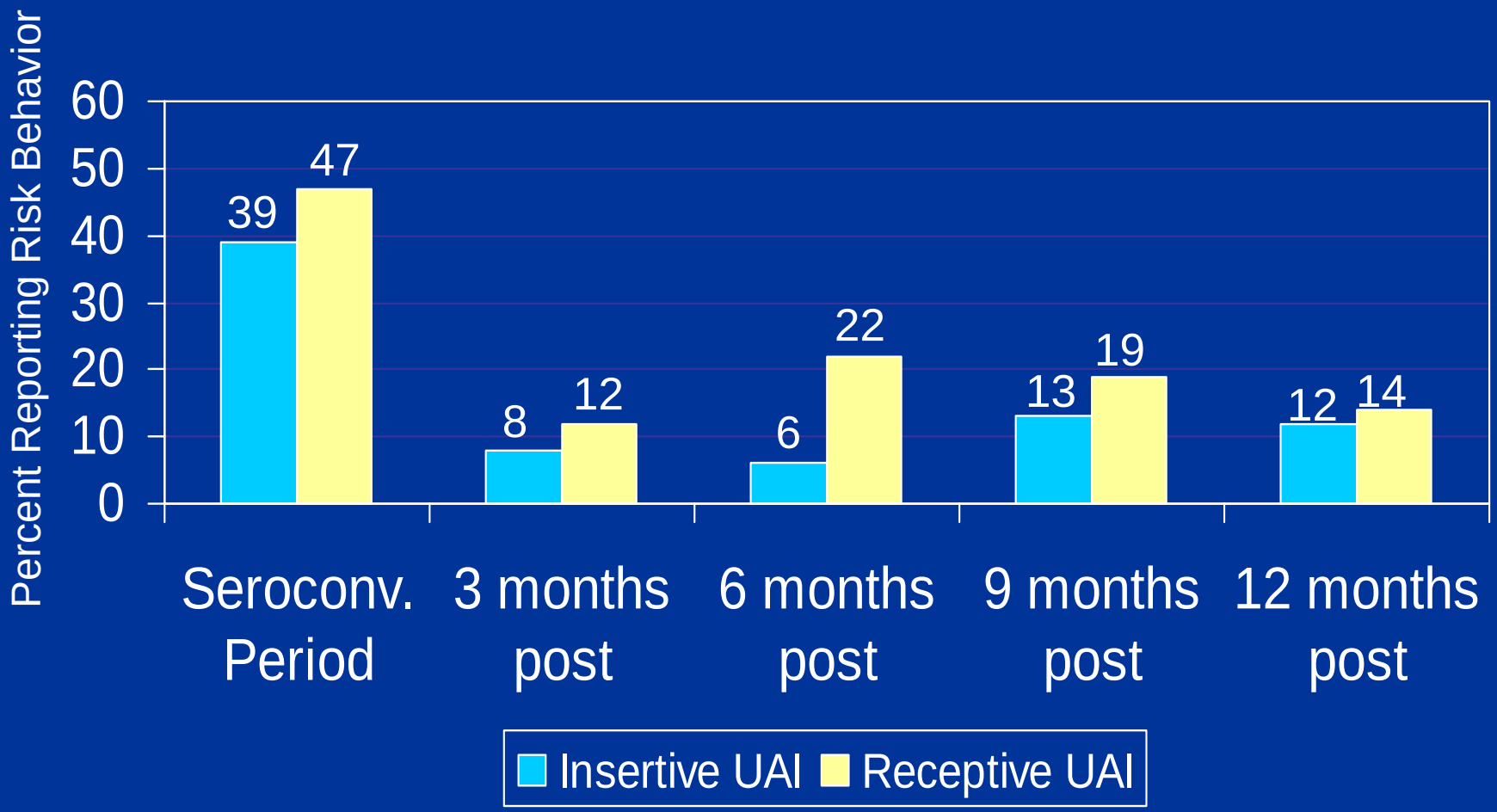
Proportion Reporting Anal Sex Behavior at Seroconversion and Post Seroconversion Visits



Source: Colfax et al, *AIDS* 2002

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AHP Strategies

- **Four priorities:**
  1. **Make voluntary HIV testing a routine part of medical care**
  2. **Implement new models for diagnosing HIV infections outside medical settings**
  3. **Prevent new infections by working with persons diagnosed with HIV and their partners**
  4. **Further decrease perinatal HIV transmission**

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Rapid HIV Testing

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Four FDA-approved Rapid HIV Tests

	Sensitivity *(95% C.I.)*	Specificity *(95% C.I.)*
OraQuick Advance		
- whole blood	99.6 *(98.5 - 99.9)*	100 *(99.7-100)*
- oral fluid	99.3 *(98.4 - 99.7)*	99.8 *(99.6 – 99.9)*
- plasma	99.6 *(98.5 - 99.9)*	99.9 *(99.6 – 99.9)*
Uni-Gold Recombigen	100 *(99.5 – 100)*	99.7 *(99.0 – 100)*
- whole blood	100 *(99.5 – 100)*	99.8 *(99.3 – 100)*
- serum/plasma		

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Four FDA-approved Rapid HIV Tests

	Sensitivity *(95% C.I.)*	Specificity *(95% C.I.)*
Reveal *G2*		
- serum	99.8 *(99.2 – 100)*	99.1 *(98.8 – 99.4)*
- plasma	99.8 *(99.0 – 100)*	98.6 *(98.4 – 98.8)*
Multispot		
- serum/plasma	100 (99.9 – 100)	99.9 (99.8 – 100)
- HIV-2	100 (99.7 – 100)	

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OraQuick Advance HIV-1/2

- CLIA-waived for finger stick, whole blood, oral fluid; moderate complexity with plasma
- Store at room temperature
- Screens for HIV-1 and 2
- Results in 20 minutes

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Obtain finger stick specimen…

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… or whole blood

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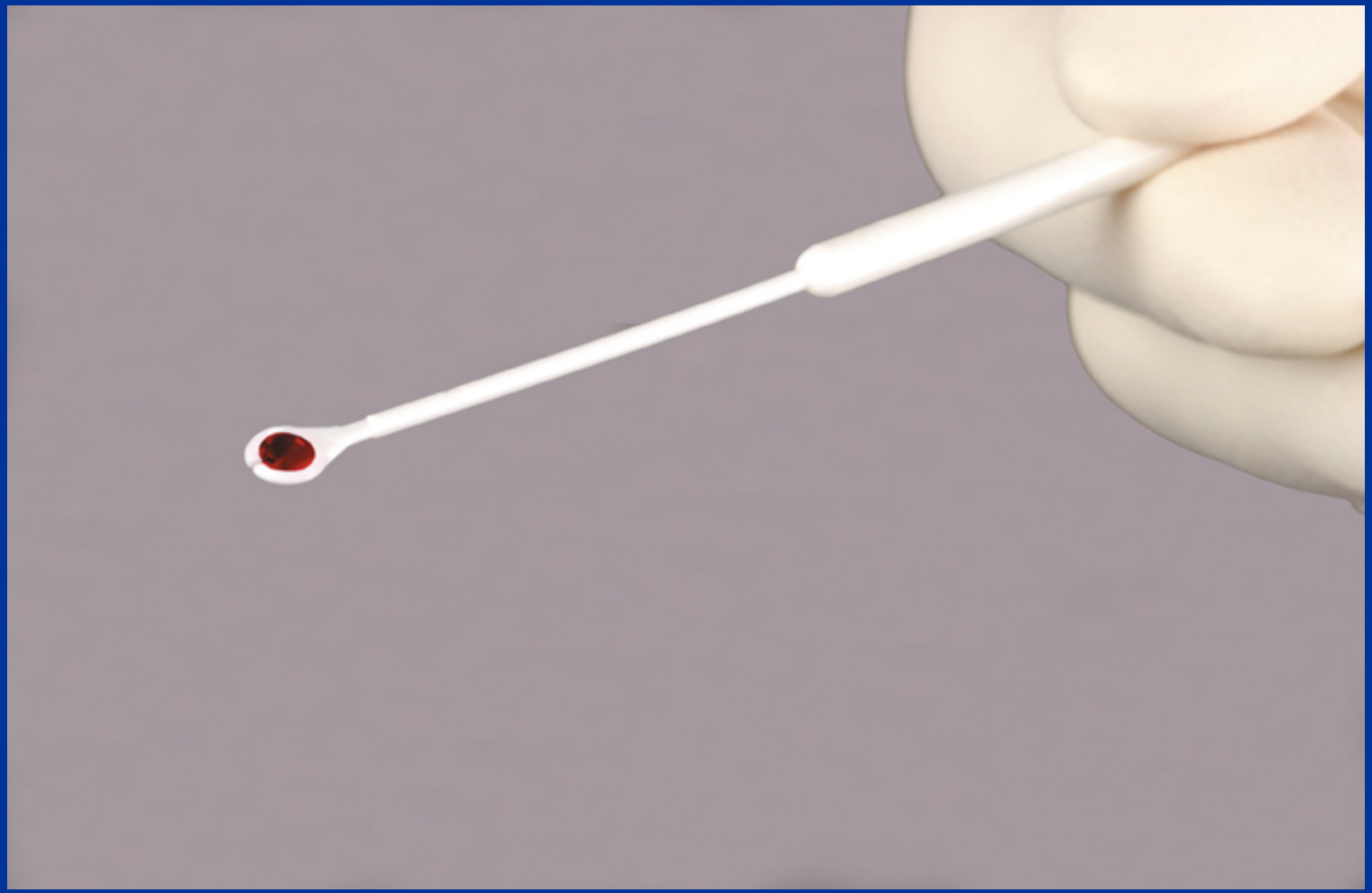

Loop collects 5 microliters of whole blood

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Insert loop into vial and stir

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Collect oral fluid specimens by swabbing gums with test device.

Reduce hazards, facilitate testing in field settings

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Insert device; test develops in 20 minutes

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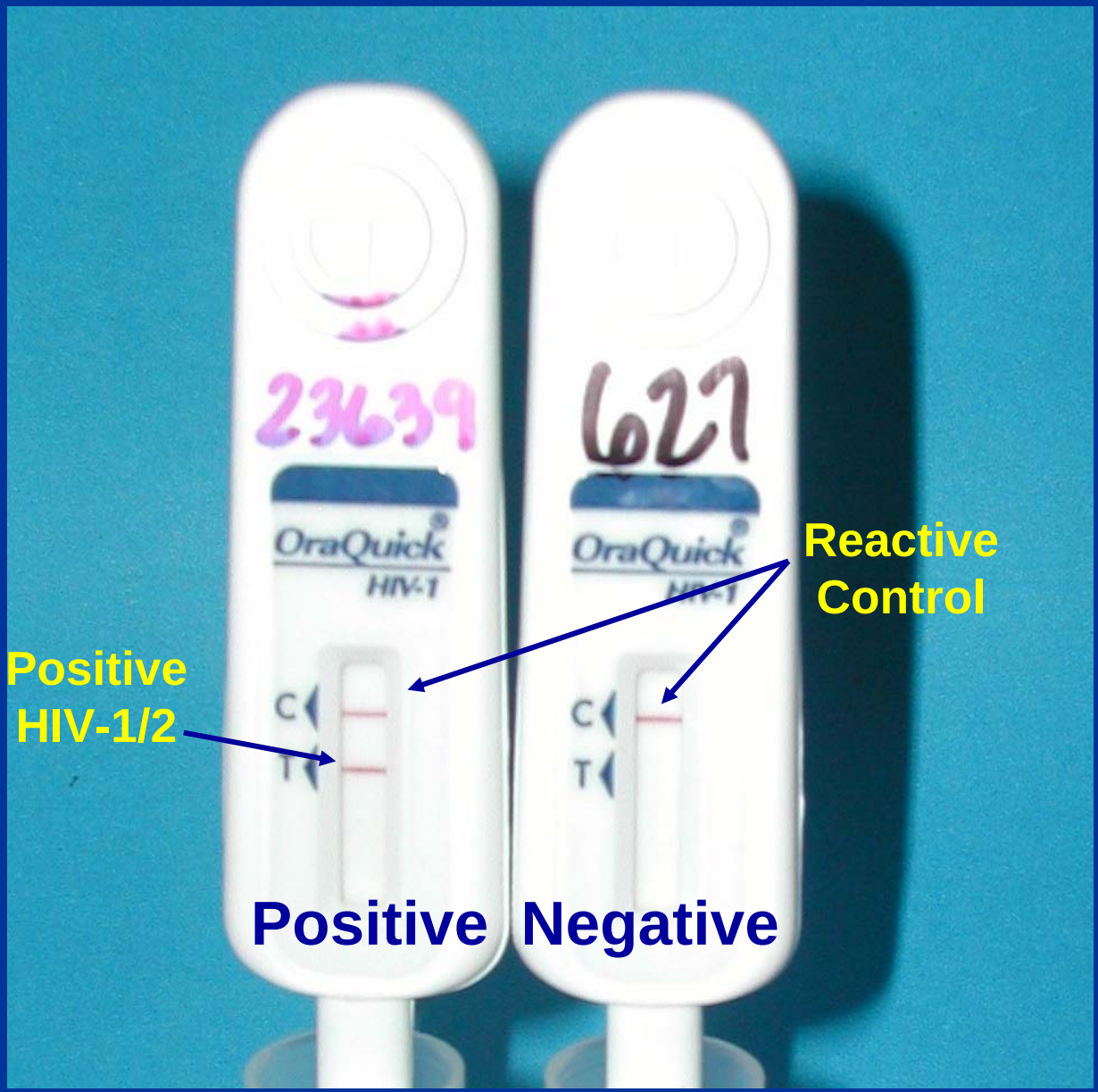

Read results in 20 – 40 minutes

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Uni-Gold Recombigen

- CLIA-waived for finger stick, whole blood; moderate complexity with serum, plasma
- Store at room temperature
- Screens for HIV-1
- Results in 10 minutes

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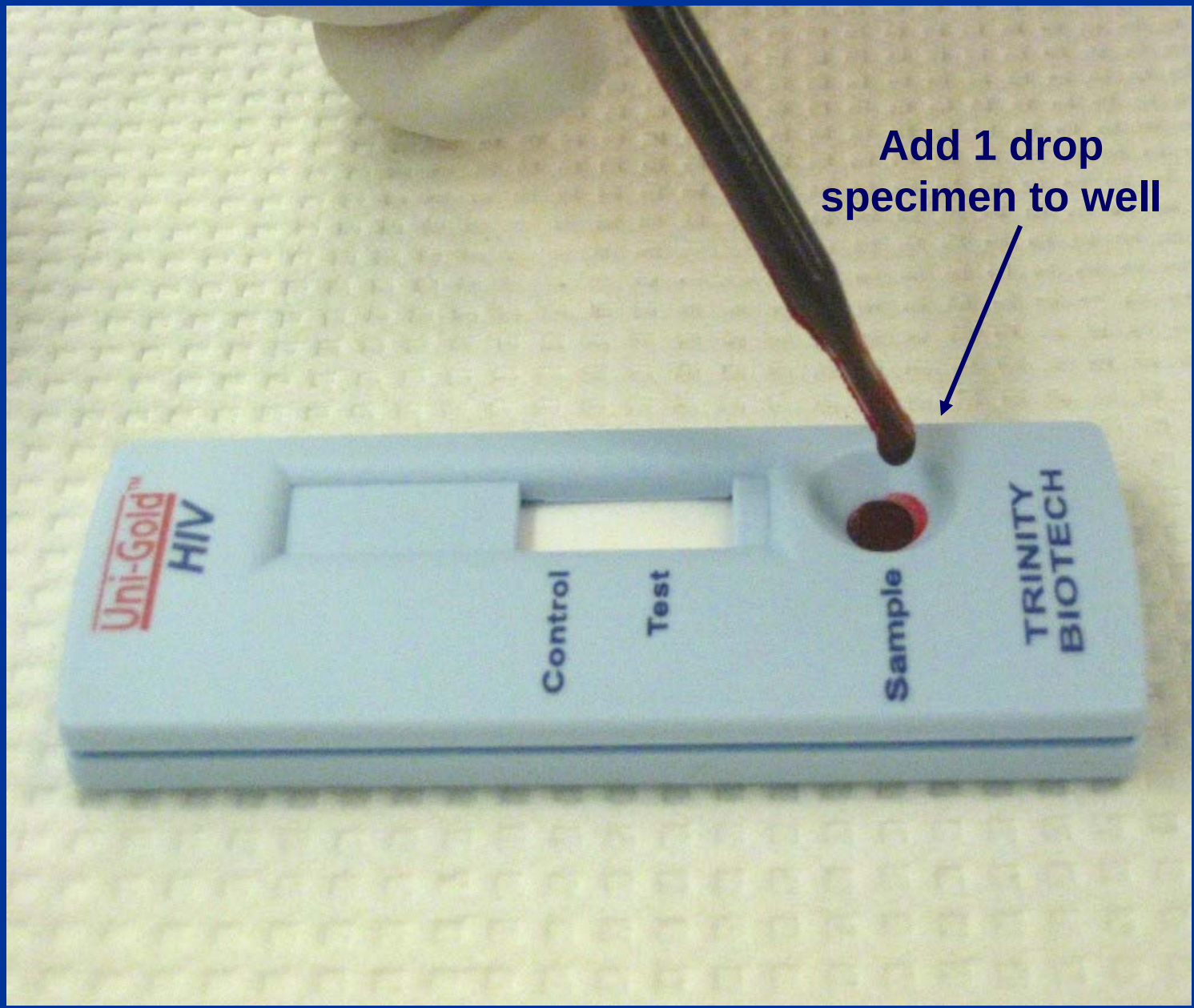

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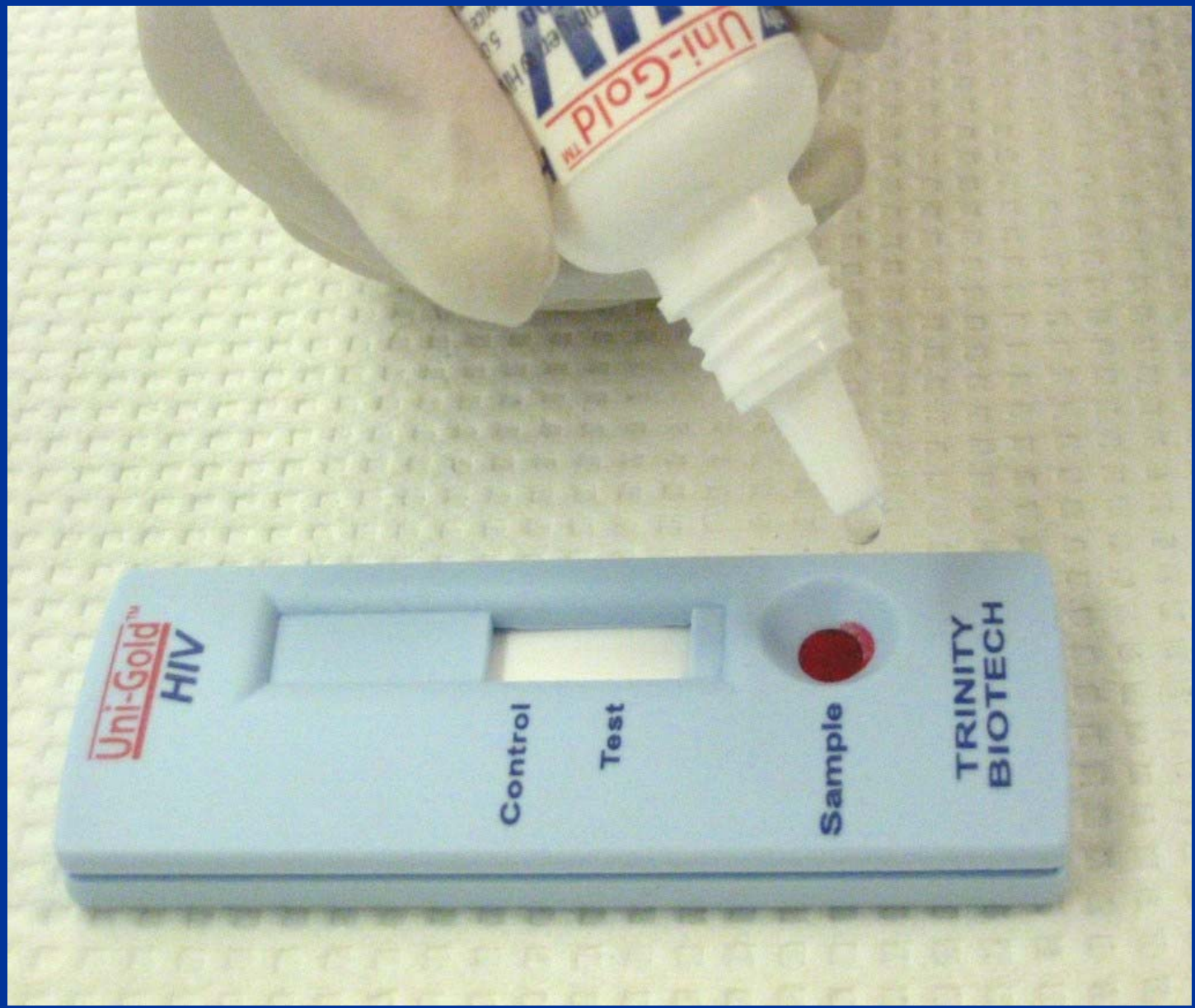

Add 4 drops of wash solution

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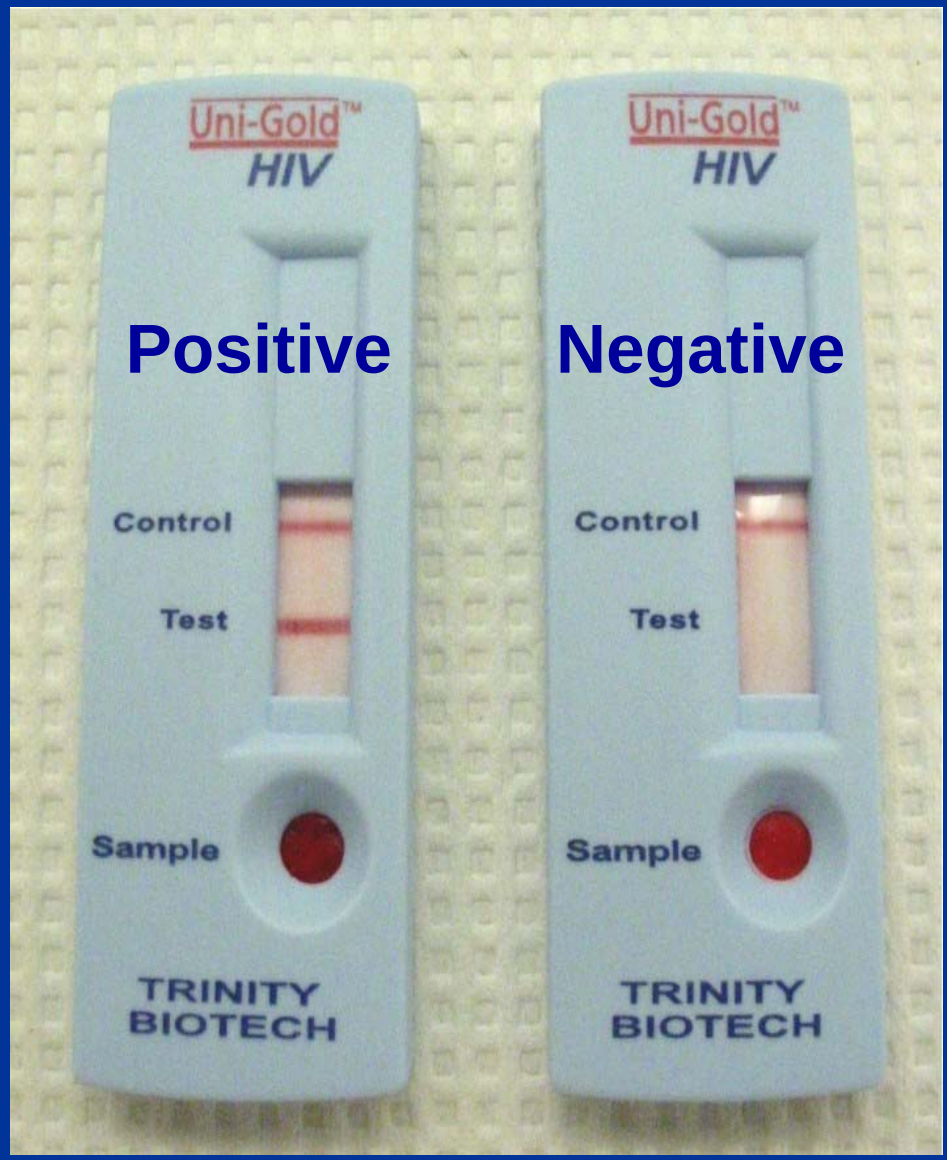

Read results in 10 minutes

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Requirements for Waived Rapid HIV Testing

- Sold only to “clinical laboratories”
- Have an adequate quality assurance program
- Assurance that operators will receive and use instructional materials

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Requirements for waived Rapid Testing

- To perform CLIA-waived tests, entities must:
  1) Enroll in CLIA program
  2) Obtain a Certificate of Waiver
  3) Pay a biennial fee
  4) Follow manufacturers' instructions
  5) Meet state requirements

- QA guidelines for waived testing and sample forms:

  www.cdc.gov/hiv/rapid_testing

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Reveal G2

- CLIA moderate complexity with serum, plasma
- Reconstitute and refrigerate reagents
- Screens for HIV-1
- Perform test in 5 minutes

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Centrifuge to obtain serum or plasma

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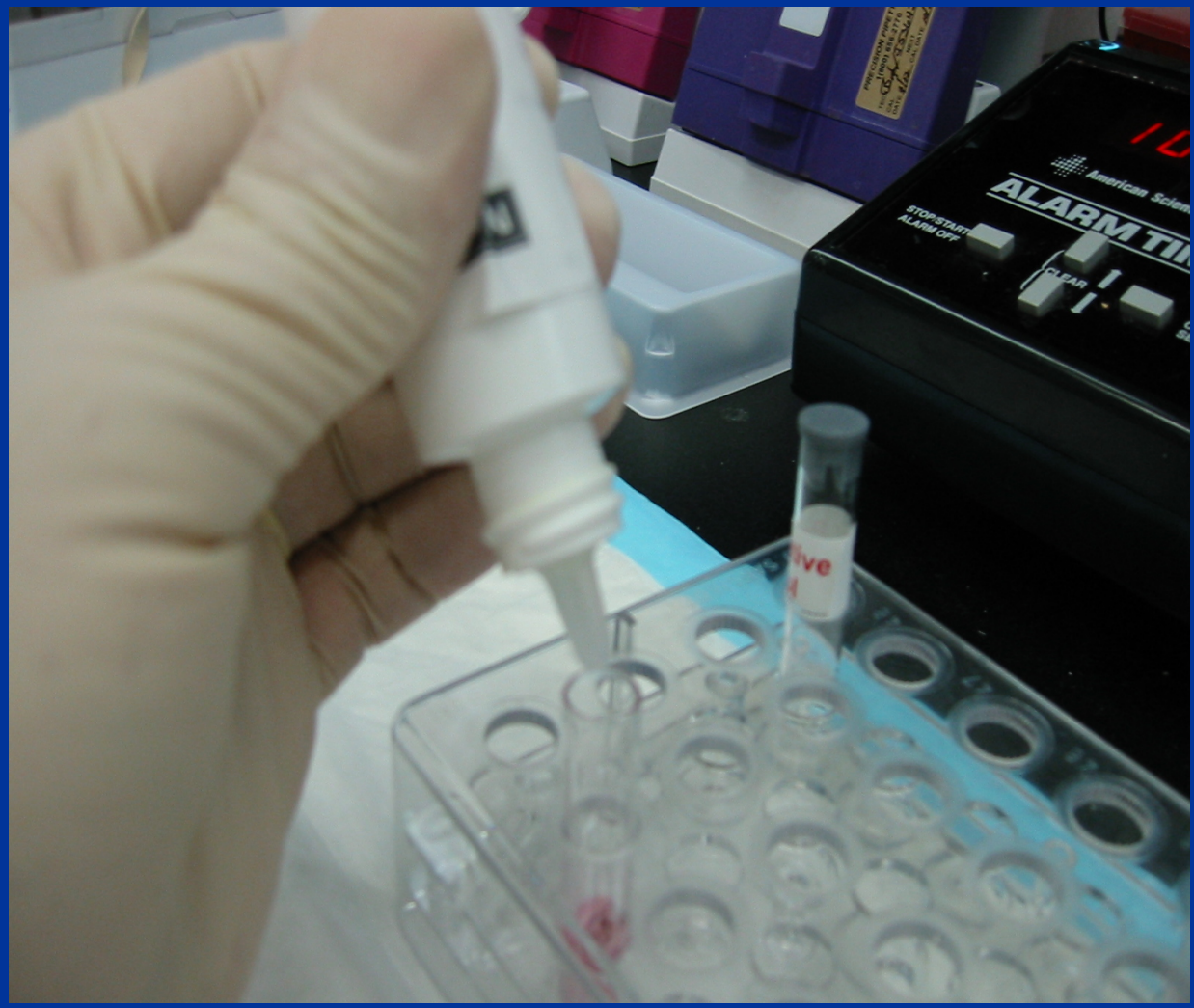

Add buffer to reconstitute conjugate.
(Sufficient for 15 tests; Refrigerate to store)

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Add 3 drops buffer to moisten membrane

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Add one drop of serum or plasma, followed by 3 drops of buffer.

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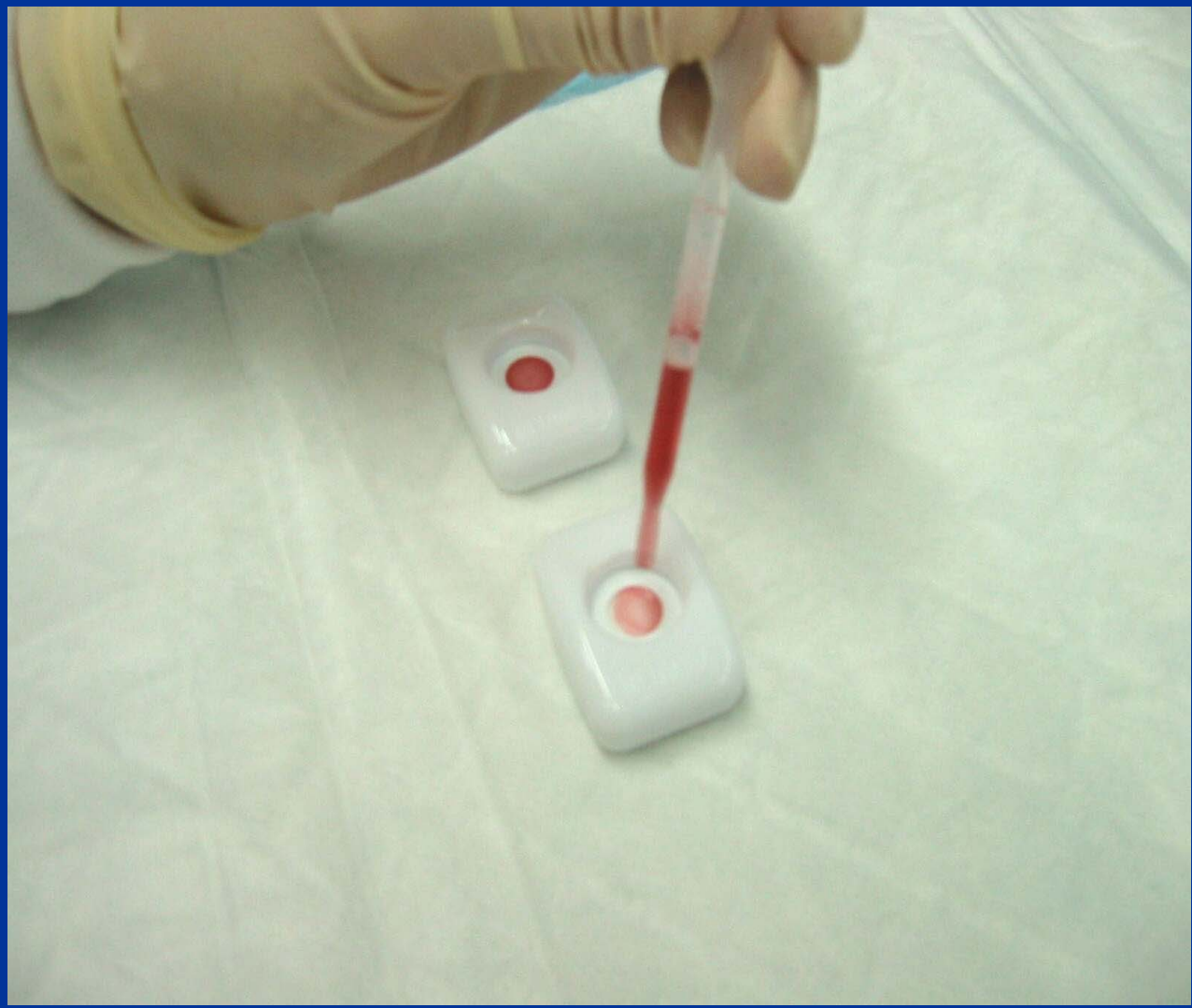

Add 4 drops of Colorimetric Detection Agent

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Add 3 drops of buffer to wash

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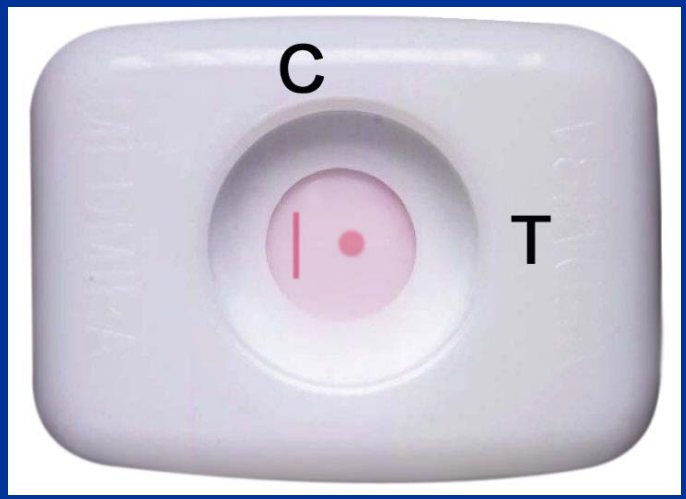

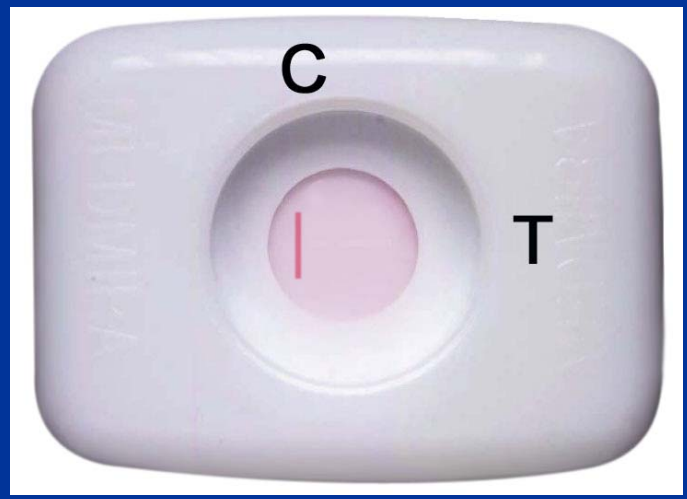

Reactive **Negative**

Read results immediately

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Multispot HIV-1/HIV-2

- CLIA moderate complexity with serum, plasma
- Refrigerate reagents
- Distinguishes HIV-1 from HIV-2
- Perform test in 15 minutes

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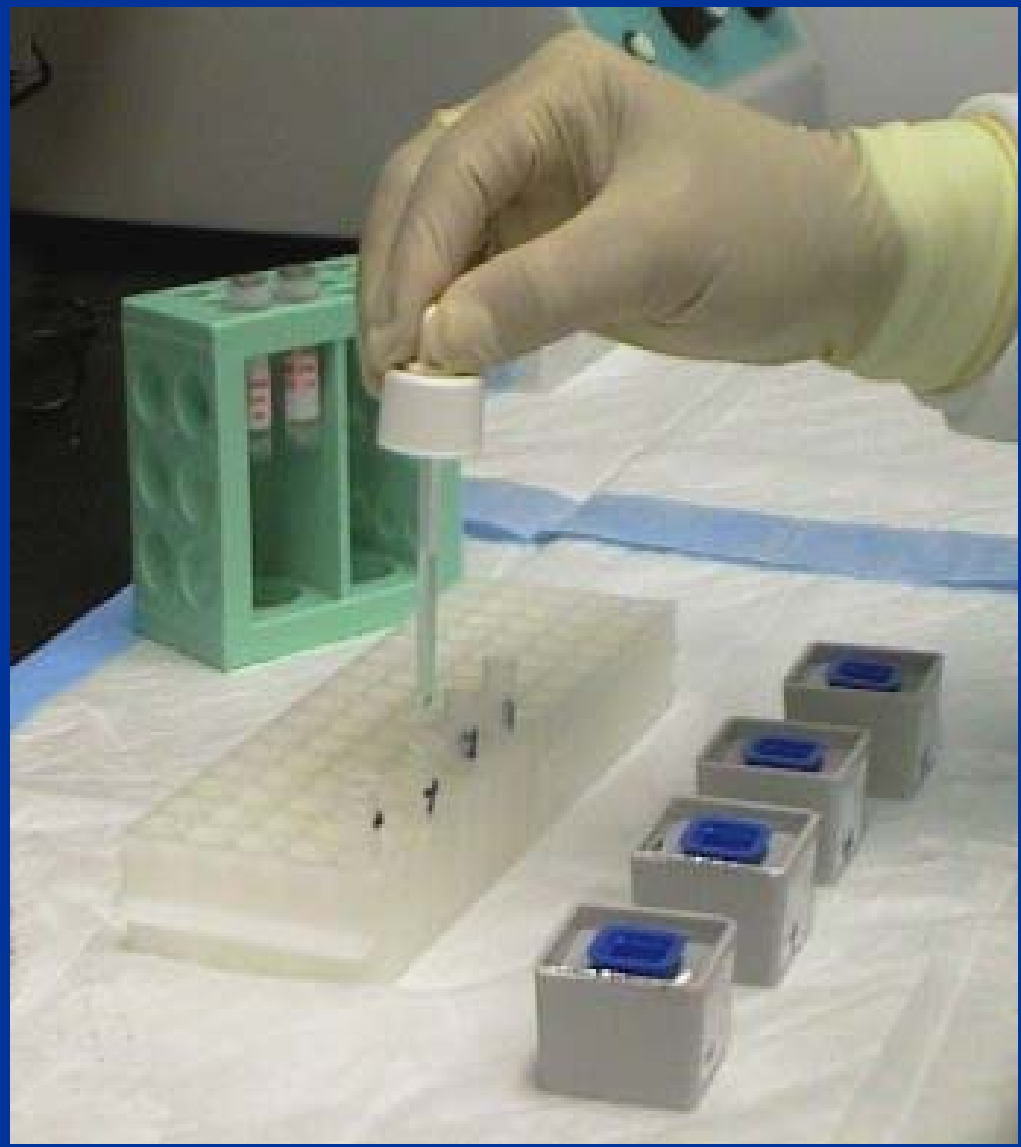

Dilute plasma or serum

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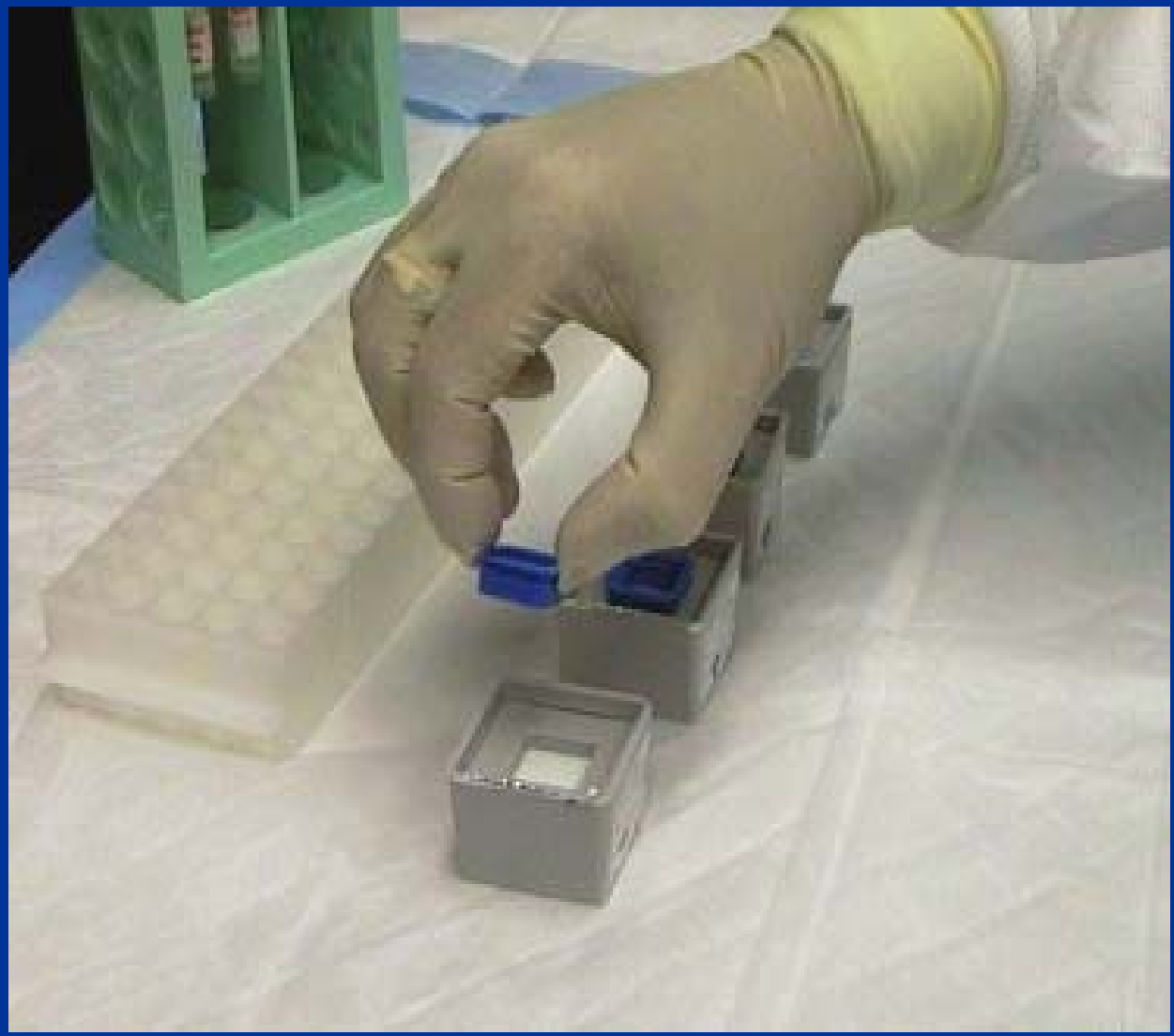

Remove and discard pre-filter

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Several timed reagent & wash steps

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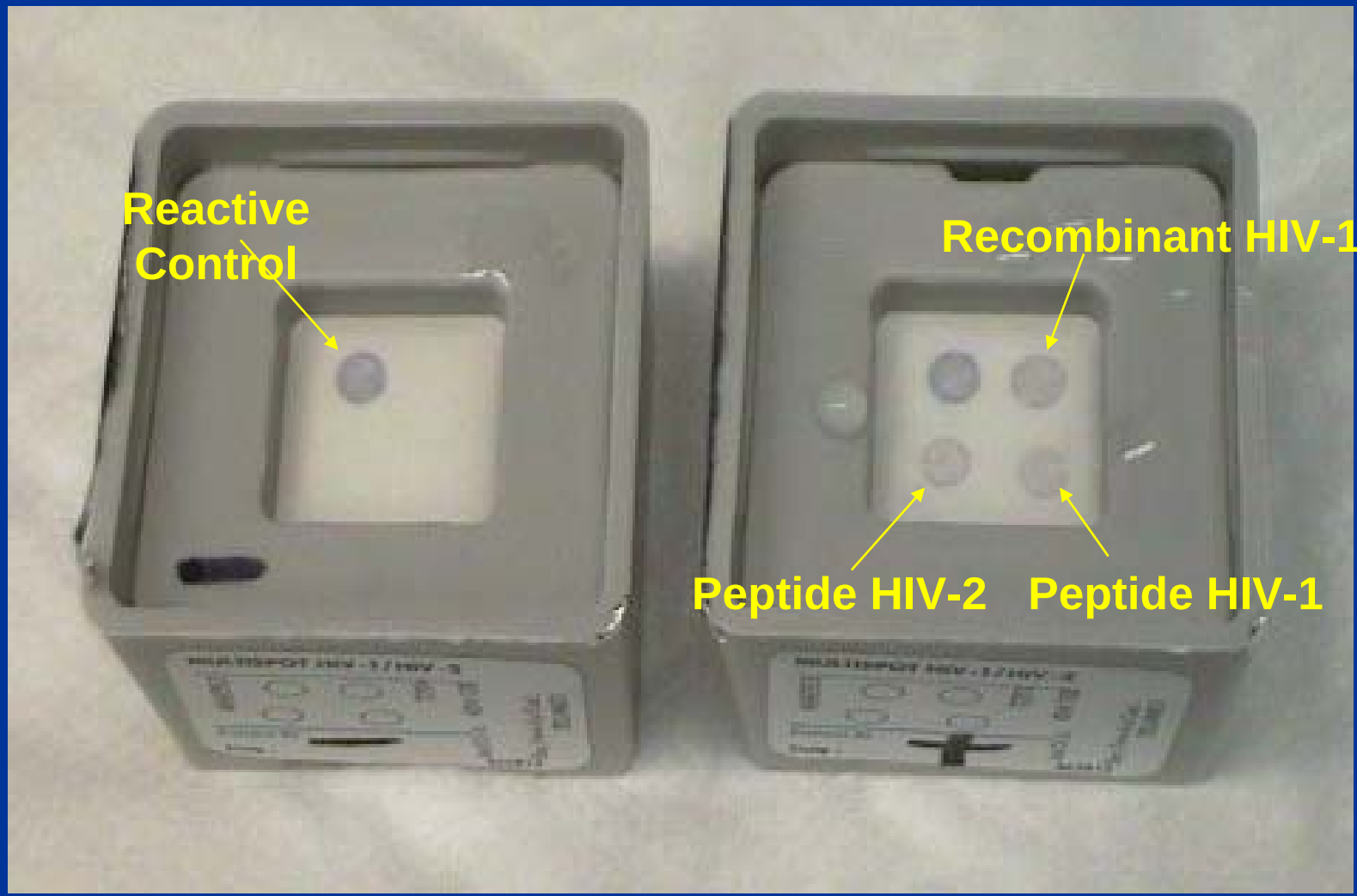

Negative

HIV-1 & HIV-2 Positive

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Point-of-Care Testing

- To expand testing in non-clinical settings:
  - Fingerstick or oral fluid specimen
  - One-step
  - Easy to interpret
  - Internal control

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Example: Three possible OraQuick test results

- Non-reactive
- Reactive
- Invalid

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Invalid

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Invalid

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Invalid

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Invalid

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The challenge: Weakly Reactive

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The Need for Training

- Blood & body fluid precautions
- Obtaining the specimen (finger stick or blood draw)
- Performing the test
- Providing test results and counseling
- OSHA requirements
- Quality assurance

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Elements of a QA Program

1. Organization of the QA Program
2. Testing Personnel
3. Process Control:
    1. Before testing
    2. During testing
    3. After testing
4. Documents and Records
5. Troubleshooting

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Process Control

Before testing	During testing	After testing
▪ Check storage and room temperatures daily ▪ Check inventory and test kit lots, as needed ▪ Receive request for testing ▪ Provide HIV/AIDS information to the test subject ▪ Set up test area, label test device ▪ Perform external quality control according to the manufacturer's and the site's instructions	▪ Follow biohazard safety precautions ▪ Collect the finger-stick specimen ▪ Perform the test ▪ Interpret test results	▪ Clean up and dispose of biohazardous waste ▪ Report results to client ▪ Document results ▪ Collect, process and transport confirmatory test specimens ▪ Manage confirmatory test results ▪ Participate in external quality assessment (periodically)

Remember the tradeoffs…

- Good News: More HIV-positive people receive their test results.
- Bad News: Some people will receive a false-positive result before confirmatory testing.

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Interpreting Rapid Test Results

For a laboratory test:

Sensitivity: Probability test=positive if patient=positive

Specificity: Probability test=negative if patient=negative

Predictive value:

Probability patient=positive if test=positive

Probability patient=negative if test=negative

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Example: Test 1,000 persons

Test Specificity = 99.6% *(4/1000)*

HIV prevalence = 10%

True positive:	100	False positive:	4

Positive predictive value: 100/104 = 96%

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Example: Test 1,000 persons

Test Specificity = 99.6% *(4/1000)*

HIV prevalence = 10%

True positive: 100 False positive: 4

Positive predictive value: 100/104 = 96%

HIV prevalence = 0.4%

True positive: 4 False positive: 4

Positive predictive value: 4/8 = 50%

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Positive Predictive Value of a Single Test Depends on Specificity & Varies with Prevalence

	Predictive Value, Positive Test			
HIV Prevalence	**OraQuick**	**Reveal**	**Uni-Gold**	**Single EIA**
10%	99%	92%	97%	98%
5%	98%	85%	95%	96%
2%	95%	69%	87%	91%
1%	91%	53%	77%	83%
0.5%	83%	36%	63%	71%
0.3%	75%	25%	50%	60%
0.1%	50%	10%	25%	33%
Test Specificity	**99.9%**	**99.1%**	**99.7%**	**99.8%**

Positive Predictive Value: Newborn Screening

	Specificity	PPV
PKU	99.7	2.65%
Galactosemia	99.7	0.57%
Hypothyroidism	98.3	1.77%
Adrenal Hyperplasia	99.0	0.53%

Newborn Screening results , 1993
Arch Pediatr Adolesc Med, July 2000

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Negative Predictive Value of a Single Test Depends on Sensitivity & Varies with Prevalence

	Predictive Value, Negative Test			
HIV Prevalence	**OraQuick**	**Reveal**	**Uni-Gold**	**Single EIA**
10%	99.96%	99.98%	100%	100%
5%	99.98%	99.99%	100%	100%
2%	99.99%	100%	100%	100%
1%	100%	100%	100%	100%
0.5%	100%	100%	100%	100%
0.3%	100%	100%	100%	100%
0.1%	100%	100%	100%	100%
Test Sensitivity	**99.6%**	**99.8%**	**100%**	**100%**

Making HIV Testing a Routine Part of Medical Care

- Cook County Hospital ED, Chicago
- OraQuick testing since Oct 02
  - 62% accept HIV testing
  - 98% receive test results
  - 3,802 patients screened
  - 93 (2.4%) new HIV positive
  - 80% entered HIV care (median 18 days)
- HIV tests ordered by ED providers increased from 5 to 29 per month

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E.D. Point-of-Care Testing

- Hospital lab:
  - Mean, 107 minutes
  - 55% of patients left before receiving test results
- ED Satellite lab:
  - Mean, 48 minutes
  - 20% of patients left before receiving test results

Kelen et al, Ann Emerg Med, 1999

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HIV Screening in Acute Care Settings

	New HIV+
Cook County ED, Chicago	2.3%
Grady ED, Atlanta	2.7%
Johns Hopkins ED, Baltimore	3.2%
HIV testing sites	*1.3%*

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L&D Point-of-Care Testing Station

- The rapid test is done on this counter, extra supplies are stored below.
- OB physicians and midwives share MIRIAD testing

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Turnaround Times for Rapid Test Results, Point-of-Care vs Lab Testing

- Point-of-care testing: median 45 min
  - (range 30 min – 2.5 hours)
- Same test in Laboratory: median 3.5 hours
  - (range 94 min – 16 hours)

MMWR 52:36, Sept 16, 2003

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Outcomes of Confirmatory Testing

Initial specimen			Follow-up specimen		
EIA*	Confirmatory test		EIA	Supplemental test	
ND†	IFA	neg§	neg	IFA¶	pos**
neg	—	ND	ND	Viral load	>750,000 copies
neg	WB††,§§	Indeterm¶¶	pos	WB	Pos
neg	WB§§	pos	ND	ND	—
neg	WB§§	pos	ND	ND	—
pos	IFA	indeterm	pos	WB	Pos
pos	WB	indeterm	pos	WB	Pos
pos	WB	indeterm	ND	Viral load	>750,000 copies
pos	WB	indeterm	pos	WB	Pos
neg	WB	neg	ND	Viral load	neg
neg	WB	indeterm	ND	WB	neg
neg	WB	neg	neg	WB	neg
neg	WB	neg	neg	WB	neg

MMWR March 19, 2004

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Results of Confirmatory Testing

OraQuick	Initial specimen			Follow-up specimen		
	EIA*	Confirmatory test		EIA	Supplemental test	
Reactive	ND†	IFA	neg§	neg	IFA¶	pos**
Reactive	neg	—	ND	ND	Viralload	>750,000 copies
Reactive	neg	WB††,§§	Indeterm¶¶	pos	WB	Pos
Reactive	neg	WB§§	pos	ND	ND	—
Reactive	neg	WB§§	pos	ND	ND	—

5 patients:

- **Initial EIA or confirmatory test negative**
- **Some labs did only EIA**
- **HIV-positive on follow-up specimen**

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Results of Confirmatory Testing

	Initial specimen			Follow-up specimen		
OraQuick	EIA*	Confirmatory test		EIA	Supplemental test	
Reactive	pos	IFA	indeterm	pos	WB	Pos
Reactive	pos	WB	indeterm	pos	WB	Pos
Reactive	pos	WB	indeterm	ND	Viral load	>750,000 copies
Reactive	pos	WB	indeterm	pos	WB	Pos

4 patients:

- **Initial confirmatory test indeterminate**
- **Early infection, evolving Western blot**
- **HIV-positive on follow-up specimen**

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Results of Confirmatory Testing

	Initial specimen			Follow-up specimen		
OraQuick	EIA*	Confirmatory test		EIA	Supplemental test	
Reactive	neg	WB	neg	ND	Viral load	neg
Reactive	neg	WB	indeterm	ND	WB	neg
Reactive	neg	WB	neg	neg	WB	neg
Reactive	neg	WB	neg	neg	WB	neg

4 patients:

- **Initial and follow-up tests negative**
- **False-positive OraQuick rapid test**

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Results of Confirmatory Testing

	Initial specimen			Follow-up specimen		
OraQuick	EIA*	Confirmatory test		EIA	Supplemental test	
Reactive	pos	WB	neg	—	—	—
Reactive	neg	WB	indeterm	—	—	—
Reactive	neg	WB	indeterm	—	—	—
Reactive	neg	WB	neg	—	—	—
Reactive	neg	WB	neg	—	—	—
Reactive	neg	WB	neg	—	—	—
Reactive	neg	WB	neg	—	—	—
Reactive	neg	WB	neg	—	—	—

8 patients:

- **Unsuccessful follow-up**
- **HIV status unconfirmed**

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Confirmatory Testing

- Confirmatory test essential (not just EIA!)
- For Western blot:
  - Venipuncture for whole blood
  - Oral fluid specimen
- Follow-up testing of persons with negative or indeterminate Western blot results after 4 weeks

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Additional Resources

General and technical information (updated frequently):

www.cdc.gov/hiv/rapid_testing

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